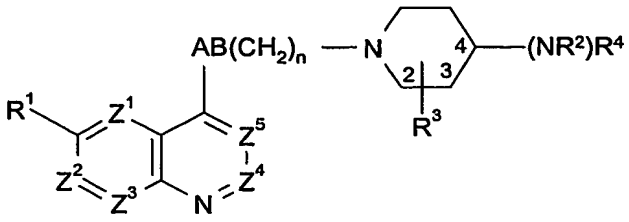
Claims

1. a compound of formula (I) or a pharmaceutically acceptable derivative thereof:



(I)

wherein:

one of Z^1, Z^2, Z^3, Z^4 and Z^5 is N, one is CR^{1a} and the remainder are CH , or one or two of Z^1, Z^2, Z^3, Z^4 and Z^5 are independently CR^{1a} and the remainder are CH;

R^1 and R^{1a} are independently hydrogen; hydroxy; (C_{1-6})alkoxy optionally substituted by (C_{1-6})alkoxy, amino, piperidyl, guanidino or amidino any of which is optionally N-substituted by one or two (C_{1-6})alkyl, acyl or (C_{1-6})alkylsulphonyl groups, $CONH_2$, hydroxy, (C_{1-6})alkylthio, heterocyclylthio, heterocyclyloxy, arylthio, aryloxy, acylthio, acyloxy or (C_{1-6})alkylsulphonyloxy; (C_{1-6})alkoxy-substituted(C_{1-6})alkyl; halogen; (C_{1-6})alkyl; (C_{1-6})alkylthio; trifluoromethyl; trifluoromethoxy; nitro; azido; acyl; acyloxy; acylthio; (C_{1-6})alkylsulphonyl; (C_{1-6})alkylsulphoxide; arylsulphonyl; arylsulphoxide or an amino, piperidyl, guanidino or amidino group optionally N-substituted by one or two (C_{1-6})alkyl, acyl or (C_{1-6})alkylsulphonyl groups;

or when Z^5 is CR^{1a}, R^{1a} may instead be cyano, hydroxymethyl or carboxy;

or R^1 and R^{1a} on adjacent positions may together form ethylenedioxy;

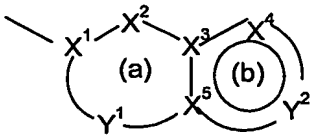
provided that when Z^1, Z^2, Z^3, Z^4 and Z^5 are CR^{1a} or CH, then R^1 is not hydrogen;

R^2 is hydrogen, or (C_{1-4})alkyl or (C_{2-4})alkenyl optionally substituted with 1 to 3 groups selected from:
amino optionally substituted by one or two (C_{1-4})alkyl groups; carboxy; (C_{1-4})alkoxycarbonyl; (C_{1-4})alkylcarbonyl; (C_{2-4})alkenyloxycarbonyl; (C_{2-4})alkenylcarbonyl; aminocarbonyl wherein the amino group is optionally substituted by hydroxy, (C_{1-4})alkyl, hydroxy(C_{1-4})alkyl, aminocarbonyl(C_{1-4})alkyl, (C_{2-4})alkenyl, (C_{1-4})alkylsulphonyl, trifluoromethylsulphonyl, (C_{2-4})alkenylsulphonyl, $(C_{1-}$

4)alkoxycarbonyl, (C_{1-4})alkylcarbonyl, (C_{2-4})alkenyloxycarbonyl or (C_{2-4})alkenylcarbonyl; cyano; tetrazolyl; 2-oxo-oxazolidinyl optionally substituted by R^{10}; 3-hydroxy-3-cyclobutene-1,2-dione-4-yl; 2,4-thiazolidinedione-5-yl; tetrazol-5-ylaminocarbonyl; 1,2,4-triazol-5-yl optionally substituted by R^{10}; 5-oxo-1,2,4-oxadiazol-3-yl; halogen; (C_{1-4})alkylthio; trifluoromethyl; hydroxy optionally substituted by (C_{1-4})alkyl, (C_{2-4})alkenyl, (C_{1-4})alkoxycarbonyl, (C_{1-4})alkylcarbonyl, (C_{2-4})alkenyloxycarbonyl, (C_{2-4})alkenylcarbonyl; oxo; (C_{1-4})alkylsulphonyl; (C_{2-4})alkenylsulphonyl; or (C_{1-4})aminosulphonyl wherein the amino group is optionally substituted by (C_{1-4})alkyl or (C_{2-4})alkenyl;

R^3 is in the 2-, 3- or 4-position and is trifluoromethyl or is in the 2-position and is oxo; or R^3 is in the 3-position and is fluorine or amino wherein the amino group is optionally substituted by: hydroxy; (C_{1-6})alkylsulphonyl; trifluoromethylsulphonyl; (C_{2-6})alkenylsulphonyl; (C_{1-6})alkylcarbonyl; (C_{2-6})alkenylcarbonyl; (C_{1-6})alkoxycarbonyl; (C_{2-6})alkenyloxycarbonyl; (C_{1-6})alkyl; or (C_{2-6})alkenyl; wherein a (C_{1-6})alkyl or (C_{2-6})alkenyl moiety may be optionally substituted with up to 2 groups R^{12} independently selected from:
halogen; (C_{1-6})alkylthio; trifluoromethyl; cyano; carboxy; tetrazolyl; 2-oxo-oxazolidinyl; 3-hydroxy-3-cyclobutene-1,2-dione-4-yl; 2,4-thiazolidinedione-5-yl; tetrazol-5-ylaminocarbonyl; 1,2,4-triazol-5-yl optionally substituted by R^{10}; or 5-oxo-1,2,4-oxadiazol-3-yl; (C_{1-6})alkoxycarbonyl; (C_{1-6})alkylcarbonyl; (C_{2-6})alkenyloxycarbonyl; (C_{2-6})alkenylcarbonyl; hydroxy optionally substituted by (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenylcarbonyl or aminocarbonyl wherein the amino group is optionally substituted by (C_{1-6})alkyl, (C_{2-6})alkenyl; amino optionally mono- or disubstituted by (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenyloxycarbonyl, (C_{2-6})alkenylcarbonyl, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkylsulphonyl, (C_{2-6})alkenylsulphonyl or aminocarbonyl wherein the amino group is optionally substituted by (C_{1-6})alkyl or (C_{2-6})alkenyl;
in addition when R^3 is disubstituted with a hydroxy or amino containing substituent and carboxy containing substituent these may together form a cyclic ester or amide linkage, respectively;

R^4 is a group -U-R^5 where
U is selected from CO, SO_2 and CH_2 and
R^5 is an optionally substituted bicyclic carbocyclic or heterocyclic ring system (A):



(A)

containing up to four heteroatoms in each ring in which

ring (a) is aromatic or non aromatic;

X^1 is C when part of an aromatic ring or CR^{14} when part of a non aromatic ring;

X^2 is N, NR^{13}, O, $S(O)_x$, CO or CR^{14} when part of an aromatic or non-aromatic ring or may in addition be $CR^{14}R^{15}$ when part of a non aromatic ring;

X^4 is N, NR^{13}, O, $S(O)_x$, CO or CR^{14};

X^3 and X^5 are independently N or C;

Y^1 is a 1 to 3 atom linker group each atom of which is independently selected from N, NR^{13}, O, $S(O)_x$, CO and CR^{14} when part of an aromatic or non-aromatic ring or may additionally be $CR^{14}R^{15}$ when part of a non aromatic ring,

Y^2 is a 2 or 3 atom linker group completing an aromatic ring, each atom of Y^2 being independently selected from N, NR^{13}, O, $S(O)_x$, CO and CR^{14};

each of R^{14} and R^{15} is independently selected from: H; (C_{1-4})alkylthio; halo; carboxy(C_{1-4})alkyl; halo(C_{1-4})alkoxy; halo(C_{1-4})alkyl; (C_{1-4})alkyl; (C_{2-4})alkenyl; (C_{1-4})alkoxycarbonyl; formyl; (C_{1-4})alkylcarbonyl; (C_{2-4})alkenyloxycarbonyl; (C_{2-4})alkenylcarbonyl; (C_{1-4})alkylcarbonyloxy; (C_{1-4})alkoxycarbonyl(C_{1-4})alkyl; hydroxy; hydroxy(C_{1-4})alkyl; mercapto(C_{1-4})alkyl; (C_{1-4})alkoxy; nitro; cyano; carboxy; amino or aminocarbonyl optionally substituted as for corresponding substituents in R^3; (C_{1-4})alkylsulphonyl; (C_{2-4})alkenylsulphonyl; or aminosulphonyl wherein the amino group is optionally mono- or di-substituted by (C_{1-4})alkyl or (C_{2-4})alkenyl; aryl; aryl(C_{1-4})alkyl; aryl(C_{1-4})alkoxy or

R^{14} and R^{15} may together represent oxo;

each R^{13} is independently H; trifluoromethyl; (C_{1-4})alkyl optionally substituted by hydroxy, (C_{1-6})alkoxy, (C_{1-6})alkylthio, carboxy, halo or trifluoromethyl; (C_{2-4})alkenyl; aryl; aryl (C_{1-4})alkyl; arylcarbonyl; heteroarylcarbonyl; (C_{1-4})alkoxycarbonyl; (C_{1-4})alkylcarbonyl; formyl; (C_{1-6})alkylsulphonyl; or aminocarbonyl wherein the amino group is optionally substituted by (C_{1-4})alkoxycarbonyl, (C_{1-4})alkylcarbonyl, (C_{2-4})alkenyloxycarbonyl, (C_{2-4})alkenylcarbonyl, (C_{1-4})alkyl or (C_{2-4})alkenyl and optionally further substituted by (C_{1-4})alkyl or (C_{2-4})alkenyl;

n is 0 or 1;

each x is independently 0, 1 or 2

A is NR^{11}, O or CR^6R^7 and B is NR^{11}, O, SO_2 or CR^8R^9 and wherein:
each of R^6, R^7, R^8 and R^9 is independently selected from: hydrogen; (C_{1-6})alkoxy; (C_{1-6})alkylthio; halo; trifluoromethyl; azido; (C_{1-6})alkyl; (C_{2-6})alkenyl; (C_{1-6})alkoxycarbonyl; (C_{1-6})alkylcarbonyl; (C_{2-6})alkenyloxycarbonyl; (C_{2-6})alkenylcarbonyl; hydroxy, amino or aminocarbonyl optionally substituted as for corresponding substituents in R^3; (C_{1-6})alkylsulphonyl; (C_{2-6})alkenylsulphonyl; or aminosulphonyl wherein the amino group is optionally substituted by (C_{1-6})alkyl or (C_{2-6})alkenyl;
or when n=1 R^6 and R^8 together represent a bond and R^7 and R^9 are as above defined;
or R^6 and R^7 or R^8 and R^9 together represent oxo;

provided that:
when A is NR^{11}, B is not NR^{11} or O;
when A is CO, B is not CO, O or SO_2;
when n is 0 and A is NR^{11}, CR^8R^9 can only be CO;
when A is CR^6R^7 and B is SO_2, n is 0;
when n is 0, B is not NR^{11} or O or R^8 and R^9 are not optionally substituted hydroxy or amino;
when A is O, B is not NR^{11}, O, SO_2 or CO and n=1; and
when A-B is $CR^7{=}CR^9$, n is 1

R^{10} is selected from (C_{1-4})alkyl; (C_{2-4})alkenyl and aryl any of which may be optionally substituted by a group R^{12} as defined above; carboxy; aminocarbonyl wherein the amino group is optionally substituted by hydroxy, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkylsulphonyl, trifluoromethylsulphonyl, (C_{2-6})alkenylsulphonyl, (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenyloxycarbonyl or (C_{2-6})alkenylcarbonyl and optionally further substituted by (C_{1-6})alkyl or (C_{2-6})alkenyl; (C_{1-6})alkylsulphonyl; trifluoromethylsulphonyl; (C_{2-6})alkenylsulphonyl; (C_{1-6})alkoxycarbonyl; (C_{1-6})alkylcarbonyl; (C_{2-6})alkenyloxycarbonyl; and (C_{2-6})alkenylcarbonyl; and

R^{11} is hydrogen; trifluoromethyl, (C_{1-6})alkyl; (C_{2-6})alkenyl; (C_{1-6})alkoxycarbonyl; (C_{1-6})alkylcarbonyl; or aminocarbonyl wherein the amino group is optionally substituted by (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenyloxycarbonyl, (C_{2-6})alkenylcarbonyl, (C_{1-6})alkyl or (C_{2-6})alkenyl and optionally further substituted by (C_{1-6})alkyl or (C_{2-6})alkenyl;

or where one of R^3 and R^6, R^7, R^8 or R^9 contains a carboxy group and the other contains a hydroxy or amino group they may together form a cyclic ester or amide linkage.

2. A compound according to claim 1 wherein Z^5 is CH, C-Cl or N, Z^3 is CH or CF and Z^1, Z^2 and Z^4 are each CH, or Z^1 is N, Z^3 is CH and Z^2 and Z^4 are each CH and Z^5 is CH or C-Cl.

3. A compound according to any preceding claim wherein R^1 is methoxy and R^{1a} is H or when Z^3 is CR^{1a} it may be C-F or when Z^5 is CR^{1a} it may be C-F or C-Cl.

4. A compound according to any preceding claim wherein R^2 is hydrogen, carboxymethyl, hydroxyethyl, aminocarbonylmethyl, ethoxycarbonylmethyl, ethoxycarbonylallyl or carboxyallyl.

5. A compound according to any preceding claim wherein R^3 is CF_3, fluoro, oxo or amino unsubstituted or substituted by (C_{1-6})alkyl or (C_{2-6})alkenyl.

6. A compound according to any preceding claim wherein n is 0, A-B is CHOH-CH_2, NR^{11}-CH_2, NR^{11}-CO or CH_2-CH_2 and R^{11} is hydrogen or (C_{1-4})alkyl.

7. A compound according to any preceding claim wherein U is CH_2 and R^5 is an aromatic heterocyclic ring (A) having 1-4 heteroatoms of which one is N or NR^{13}, R^{13} is H if in ring (a) or in addition (C_{1-4})alkyl if in ring (b), R^{14} and R^{15} are independently selected from hydrogen, halo, hydroxy, (C_{1-4})alkyl, (C_{1-4})alkoxy, trifluoromethoxy, nitro, cyano, aryl(C_{1-4})alkoxy and (C_{1-4})alkylsulphonyl.

8. A compound according to any of claims 1 to 6 wherein R^5 is 4,6-difluoro-indol-2-yl, 1H-pyrrolo[2,3-b]-pyridin-2-yl, 1H-pyrrolo[3,2-b]-pyridin-2-yl,, 8-hydroxy-quinolin-2-yl, quinoxalin-2-yl, benzimidazol-2-yl, benzo[1,2,3]-thiadiazol-5-yl, benzothiophen-2-yl, 4,6-difluoro-1H-benzimidazol-2-yl, benzothiazole-5-yl, 3-(R)-2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-3-yl or [1,2,3]thiadiazolo[5,4-b]pyridin-6-yl.

9. A compound according to claim 1 selected from:
6-[({(3*S*,4*R*)-3-fluoro-1-[(*R*)-2-hydroxy-2-(6-methoxyquinolin-4-yl)-ethyl]piperidin-4-ylamino}methyl)]- [1,2,3]thiadiazolo[5,4-b]pyridine and 6-[({(3*R*,4*S*)-3-fluoro-1-[(*R*)-2-hydroxy-2-(6-methoxyquinolin-4-yl)-ethyl]piperidin-4-ylamino}methyl)]-[1,2,3]thiadiazolo[5,4-b]pyridine;

5-[({(3*S*,4*R*)-3-fluoro-1-[(*R*)-2-hydroxy-2-(6-methoxyquinolin-4-yl)-ethyl]piperidin-4-ylamino}methyl)]- benzo[1,2,3]thiadiazole and 5-[({(3*R*,4*S*)-3-fluoro-1-[(*R*)-2-hydroxy-2-(6-methoxyquinolin-4-yl)-ethyl]piperidin-4-ylamino}methyl)]- benzo[1,2,3]thiadiazole; {3-Fluoro-1-[(R)-2-hydroxy-2-(6-methoxy-[1,5]naphthyridin-4-yl)-ethyl]-piperidin-4-yl}-[1,2,3]thiadiazolo[5,4-b]pyridin-6-ylmethyl-amine Diastereoisomer 1;
or a pharmaceutically acceptable derivative thereof.

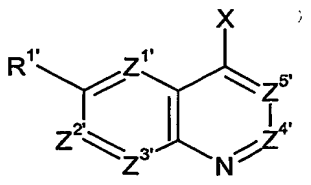
10. A method of treatment of bacterial infections in mammals, particularly in man, which method comprises the administration to a mammal in need of such treatment an effective amount of a compound according to claim 1.

11. The use of a compound according to claim 1, in the manufacture of a medicament for use in the treatment of bacterial infections in mammals.

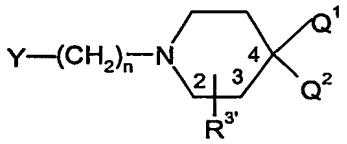
12. A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier.

13. A process for preparing compounds according to claim 1, which process comprises:

reacting a compound of formula (IV) with a compound of formula (V):



(IV)



(V)

wherein n is as defined in formula (I); $Z^{1'}$, $Z^{2'}$, $Z^{3'}$, $Z^{4'}$, $Z^{5'}$, $R^{1'}$ and $R^{3'}$ are Z^1, Z^2, Z^3, Z^4, Z^5, R^1 and R^3 as defined in formula (I) or groups convertible thereto;
Q^1 is $NR^{2'}R^{4'}$ or a group convertible thereto wherein $R^{2'}$ and $R^{4'}$ are R^2 and R^4 as defined in formula (I) or groups convertible thereto and Q^2 is H or $R^{3'}$ or Q^1 and Q^2 together form an optionally protected oxo group;
and X and Y may be the following combinations:

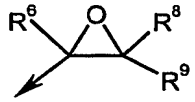
(i) X is A'-COW, Y is H and n is 0;

(ii) X is $CR^6{=}CR^8R^9$, Y is H and n is 0;

(iii) X is oxirane, Y is H and n is 0;

(iv) X is N=C=O and Y is H and n is 0;
(v) one of X and Y is CO_2R^y and the other is $CH_2CO_2R^x$;
(vi) X is CHR^6R^7 and Y is $C(=O)R^9$;
(vii) X is $CR^7=PR^z_3$ and Y is $C(=O)R^9$ and n=1;
(viii) X is $C(=O)R^7$ and Y is $CR^9=PR^z_3$ and n=1;
(ix) Y is COW and X is $NHR^{11'}$ or $NR^{11'}COW$ and n=0 or 1 or when n=1 X is COW and Y is $NHR^{11'}$ or $NR^{11'}COW$;
(x) X is $C(O=)R^6$ and Y is $NHR^{11'}$ or X is $NHR^{11'}$ and Y is $C(=O)R^8$ and n=1;
(xi) X is $NHR^{11'}$ and Y is CR^8R^9W and n=1;
(xii) X is CR^6R^7W and Y is $NHR^{11'}$ or OH and n=1;
(xiii) X is $CR^6R^7SO_2W$ and Y is H and n=0;
(xiv) X is W or OH and Y is CH_2OH and n=1;
(xv) X is $NHR^{11'}$ and Y is SO_2W or X is $NR^{11'}SO_2W$ and Y is H, and n=0;
(xvi) X is $NR^{11'}COCH_2W$ or $NR^{11'}SO_2CH_2W$ and Y is H and n=0;
(xvii) X is W and Y is $CONHR^{11'}$;

in which W is a leaving group, e.g. halo or imidazolyl; R^x and R^y are (C_{1-6})alkyl; R^z is aryl or (C_{1-6})alkyl; A' and $NR^{11'}$ are A and NR^{11} as defined in formula (I), or groups convertible thereto; and oxirane is:



wherein R^6, R^8 and R^9 are as defined in formula (I);
and thereafter optionally or as necessary converting Q^1 and Q^2 to $NR^{2'}R^{4'}$; converting A', $Z^{1'}$, $Z^{2'}$, $Z^{3'}$, $Z^{4'}$, $Z^{5'}$, $R^{1'}$, $R^{2'}$, $R^{3'}$, $R^{4'}$ and $NR^{11'}$ to A, Z^1, Z^2, Z^3, Z^4, Z^5, R^1, R^2, R^3, R^4 and $NR^{11'}$; converting A-B to other A-B, interconverting R^1, R^2, R^3 and/or R^4, and/or forming a pharmaceutically acceptable derivative thereof.